more than 1000 mL of total discharge from the chest drains. The secondary endpoint was a composite of cardiovascular death, myocardial infarction, and repeat revascularization. All patients discontinued aspirin 7 days before surgery. The night before surgery, they received either 300 mg of aspirin or placebo. Starting 6 hours postoperatively, a daily 300 mg dose of aspirin was continued in all patients. The study results in the aspirin group revealed a significant increase in postoperative bleeding and a long-term hazard decrease of nonfatal coronary events (myocardial infarction and repeat revascularization). We wish to point out a few confounders and current antiplatelet therapy issues that we believe readers should consider when interpreting the study results.

As acknowledged by the authors, the contemporary cardiac surgery practice encourages aspirin administration up until surgery. We noted that one quarter of the patients had undergone percutaneous coronary intervention 4 months (range, 2-10) before surgery. The recommendation guidelines for antiplatelet therapy after percutaneous coronary intervention suggest that most of those patients were receiving dual antiplatelet therapy after undergoing that procedure.[2] The authors do not mention if the patients were taking thienopyridines before surgery. If they were taking theinopyridines, how many days before surgery were they told to stop taking them? We consider this of great importance for the study end points because theinopyridines have a much greater influence on postoperative bleeding than aspirin.

A major confounder in the present study we consider to be the lack of platelet response to aspirin quantification. Recent evidence has shown significant individual variability in the response to aspirin and its link to outcomes.[3] The terms ''aspirin resistance'' and ''high on-treatment residual platelet reactivity'' have been introduced. Accordingly, the reported prevalence of ''aspirin resistance'' varies widely from less than 1% to 61%.[4] Platelet function tests, such as whole blood platelet aggregometry and impedance aggregometry, quantify the aspirin response. Just recently, we published a study addressing the prevalence of ''aspirin resistance'' using a point-of-care platelet function analyzer in a coronary artery bypass grafting population.[5] According to the platelet function results, individually tailored dose-dependent aspirin therapy could be recommended to reduce adverse effects (eg, bleeding) and preserve the beneficial effects. Continuous aspirin therapy up until surgery could prevent preoperative ischemic events, particularly in the residual platelet reactivity population. Preoperative discontinuation could be advised for those with a pronounced response to aspirin.

Although it is most likely true that patients taking preoperative aspirin bleed more than the patients who discontinued aspirin and that the incidence of the long-term composite of cardiovascular death, myocardial infarction, and repeat revascularization could be reduced, it is important to keep in perspective the limitations of this study. Additional research and implementation of platelet function tests in everyday clinical practice will only improve patient management and, hopefully, reduce morbidity and mortality.

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Reply to the Editor:

We would like to thank Kopjar and colleagues[1] for their interest in our study and comments on our report. Our study definitely shows that preoperative aspirin use increases postoperative bleeding but simultaneously provides some data to support the belief that it might be acceptable because of the improved long-term outcome.[2]

As rightly raised by Kopjar and colleagues,[1] aspirin resistance constitutes a major issue in modern cardiology and cardiac surgery. Its effect on clinical outcome has been established in many studies.[3] The number of aspirin nonresponders and weak responders after coronary artery bypass surgery is estimated to be quite high.[4] That we did not assess platelet function could, therefore, be considered a major limitation of the study. However, the beauty of a randomized design is that, by definition, it equalizes the confounders in both treatment arms. It is even more so when a study is double blinded and placebo controlled, as ours was. Thus, we believe the results of our study are sound and valid, even if the ''aspirin resistance'' was not assessed.

In addition, the increased bleeding incidence in patients receiving aspirin preoperatively in our study has

confirmed that aspirin was effective in at least some of them. In fact, resistance to aspirin in some patients might have actually hindered the real mean difference in bleeding and reduced the apparent long-term benefit of preoperative aspirin administration among the responders.

The separate unresolved issue remains the choice of platelet function assay to use in clinical practice and clinical trials. Let us finish by citing the conclusions of a unique report by Lordkipanidze and colleagues,[5] who compared in the same population 6 major different methods used to test platelet function: ''… conclusions drawn could be highly dependent on the test used and results from various assays are clearly not interchangeable. Hence, the clinical usefulness of the different platelet function tests to detect appropriately aspirin resistant patients remains uncertain.''

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SARCOIDOSIS—NO BUSINESS OF THE BRONCHOSCOPIST

To the Editor:

We read with interest the report ''Prospective study of endobronchial ultrasound-guided transbronchial needle aspiration of lymph nodes versus transbronchial lung biopsy of lung tissue for diagnosis of sarcoidosis'' by Oki and colleagues,[1] which appeared in the June issue of the *Journal*. While congratulating them for their effort in clarifying this controversial and relevant topic, we want to share some significant concerns we had as we read their report.

Our first concern pertains to the selection of patients. To be valid, a diagnostic study should include patients with diagnostic uncertainty. This is, in part, because patients with an obvious diagnosis do not need diagnostic tests. Although the authors included patients with suspected stage I or II sarcoidosis (excluding those with biopsy proven disease), it is unclear whether they included consecutive patients or not. If they did not include consecutive patients by filtering out some individuals, it becomes crucial to know how many and why these patients were excluded. We believe their study could potentially have a spectrum bias, overestimating the diagnostic power of the test by including target-positive patients.[2]

Other potential problems in the validity of the study by Oki and colleagues[1] could also be inflating the results. One of these is that the tests being studied were a part of the reference standard.[3] That explains why the specificities for both tests were 100%. All patients who had epithelioid cell granulomas were considered to have sarcoidosis using the clinical, radiologic, and pathologic criteria used as the reference standard. Although it is true a single reference standard is not available for sarcoidosis and a multidisciplinary meeting is recommended, a blind assessment from the adjudicators of outcome would have been preferred. It is not stated in their report who adjudicated the diagnosis.

The lack of randomization regarding the order of the tests also raises a concern. This was acknowledged by the authors in their discussion. We can think of a few potential biases from performing endobronchial ultrasonography first in every patient, and there might be many other biases that we have not considered. Randomizing the order of the tests would have been a great addition to the study protocol and would have decreased the chances of bias toward 1 procedure or the other. In addition, before the era of chest computed tomography, when mainly chest radiography was used to classify a patient as having stage I, transbronchial biopsy had a greater diagnostic yield.[4] Currently, with high-resolution computed tomography of the chest widely available, the yield of transbronchial biopsy is understandably lower.[5]

As a final comment, we have to discuss the applicability of the data. Most patients included in the trial had stage I sarcoidosis. Physicians reading their report might leave with the message that all patients with suspected stage I sarcoidosis should undergo biopsy. We believe that because a bronchoscopy can be done does not mean it should be done. The decision to establish the diagnosis of sarcoidosis should remain in the domain of the clinician caring for the patient and not the bronchoscopist.

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